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DOCKET NO: L0624.70000US00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE


Applicant: Ya Fang Liu  
Serial No: 09/156,367  
Confirmation No: 9992  
Filed: September 17, 1998  
For: METHOD FOR IDENTIFYING JNK AND MLK  
INHIBITORS FOR TREATMENT OF NEUROLOGICAL  
CONDITIONS

Examiner: Marianne P. Allen  
Art Unit: 1631

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**CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)**

The undersigned hereby certifies that this document is being placed in the United States mail with first-class postage attached, addressed to MAIL STOP RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the 7<sup>th</sup> day of April, 2004.

  
Melissa L.B. Lyons

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MAIL STOP RCE  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**STATEMENT FILED PURSUANT TO THE DUTY OF  
DISCLOSURE UNDER 37 CFR §§1.56, 1.97 AND 1.98**

Sir:

Pursuant to the duty of disclosure under 37 C.F.R. §§1.56, 1.97 and 1.98, the Applicant requests consideration of this Information Disclosure Statement.

**PART I: Compliance with 37 C.F.R. §1.97**

This Information Disclosure Statement has been filed before the mailing of a first Office Action after the filing of a request for continued examination under 37 C.F.R. §1.114.

No fee or certification is required.

**PART II: Information Cited**

The Applicant hereby makes of record in the above-identified application the information listed on the attached form PTO-1449 (modified). The order of presentation of the references should not be construed as an indication of the importance of the references.

The Applicant hereby makes the following additional information of record in the above-identified application.

The applicant would like to bring to the Examiner's attention the following co-pending applications that may contain subject matter related to this application:

<u>Serial No.</u>	<u>Filing Date</u>	<u>Inventor(s)</u>
09/886,964	June 21, 2001	Ya Fang Liu
10/042,614	January 9, 2002	Ya Fang Liu
10/360,463	February 5, 2003	Ya Fang Liu

**PART III: Remarks**

Documents cited anywhere in the Information Disclosure Statement are enclosed unless otherwise indicated. It is respectfully requested that:

1. The Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims;
2. The enclosed form PTO-1449 be signed by the Examiner to evidence that the cited information has been fully considered by the Patent and Trademark Office during the examination of this application;
3. The citations for the information be printed on any patent which issues from this application.

By submitting this Information Disclosure Statement, the Applicant makes no representation that a search has been performed, of the extent of any search performed, or that more relevant information does not exist.

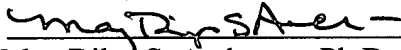
By submitting this Information Disclosure Statement, the Applicant makes no representation that the information cited in the Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. §1.56(b).

By submitting this Information Disclosure Statement, the Applicant makes no representation that the information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 U.S.C. §102.

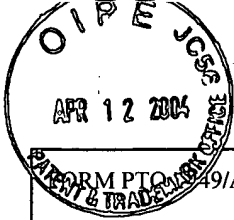
Notwithstanding any statements by the Applicant, the Examiner is urged to form his own conclusion regarding the relevance of the cited information.

An early and favorable action is hereby requested.

Respectfully submitted,  
Ya Fang Liu, *Applicant*

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Docket No. L0624.70000US00  
Date: April 7, 2004  
XNDDX



INFORMATION DISCLOSURE STATEMENT BY APPLICANT				APPLICATION NO.: 09/156,367		ATTY. DOCKET NO.: L0624.70000US00	
				FILING DATE: September 17, 1998		CONFIRMATION NO.: 9992	
				APPLICANT: Ya Fang Liu			
				GROUP ART UNIT: 1631		EXAMINER: Marianne P. Allen	
Sheet	1	of	3				

#### U.S. PATENT DOCUMENTS

Examiner's Initials	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication or of issue of Cited Document MM-DD-YYYY
		Number	Kind Code		
	AD	4,980,281		Gerard M. Housey	12-25-1990
	AE	5,385,915		Joseph D. Buxbaum et al.	01-31-1995
	AF	5,461,146		Michael E. Lewis et al.	10-24-1995
	AG	5,468,872		Marcie A. Glicksman et al.	11-21-1995
	AH	5,475,110		Robert L. Hudkins et al.	12-12-1995
	AI	5,516,772		Marcie A. Glicksman et al.	05-14-1996
	AJ	5,534,426		Michael Karin et al.	07-09-1996
	AK	5,554,523		Usharani Reddy et al.	09-10-1996
	AA2	5,750,555		Uwe Trostmann et al.	05-12-1998
	AB2	5,817,479		Janice Au-Young et al.	10-06-1998
	AC2	5,591,855		Robert L. Hudkins et al.	01-07-1997
	AD2	5,593,884		Michael Karin et al.	01-14-1997
	AE2	5,594,009		Robert L. Hudkins et al.	01-14-1997
	AF2	5,605,808		Michael Karin et al.	02-25-1997
	AG2	5,676,945		Usharani Reddy et al.	10-14-1997
	AH2	5,705,511		Robert L. Hudkins et al.	01-06-1998
	AI2	5,756,494		Michael E. Lewis et al.	05-26-1998
	AJ2	6,127,401		Jasbir Singh et al.	10-03-2000
	AK2	6,159,948		George S. Robertson et al.	12-12-2000
	AA3	6,455,525		Jasbir Singh et al.	09-24-2002
	AB3	6,514,745	B1	Michael Karin et al.	02-04-2003
	AC3	2002-0028815		Mark A. Ator et al.	03-07-2002
	AD3	2002-0061920		Diane E. Gingrich et al.	05-23-2002
	AE3	2002-0198219		Elfrida R. Grant et al.	12-26-2002

#### FOREIGN PATENT DOCUMENTS

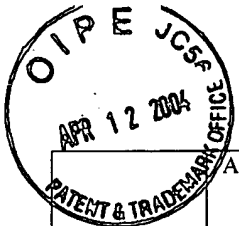
Examiner's Initials	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document (not necessary)	Date of Publication of Cited Document MM-DD-YYYY	Translation (Y/N)
		Office/ Country	Number	Kind Code			
	AM	CA	2,148,898		The General Hospital Corporation et al.	05-08-1995	
	AN	WO	93/15201		New England Deaconess Hospital	08-05-1993	
	AO	WO	94/17498		Enco-Tone Ltd.	08-04-1994	
	AP	WO	95/03324		The Regents of the University of California	02-02-1995	
	AQ	WO	95/23849		The Children's Hospital of Philadelphia	09-08-1995	



AL2	WO	99/58982		Ya Fang Liu	11-18-1999	
AM2	WO	00/13015		Cephalon, Inc.	03-09-2000	
AN2	WO	00/47583		Cephalon, Inc.	08-17-2000	
AO2	WO	02/14536		Cephalon, Inc.	02-21-2002	

# **OTHER ART — NON PATENT LITERATURE DOCUMENTS**

Examiner's Initials	Cite No	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)
	AZ4	Angeles, T. et al., Enzyme-linked Immunosorbent Assay for trkA Tyrosine Kinase Activity. Analytical Biochemistry, 236: 49-55, 1996.	
	AR5	Bergeron et al., Inhibition of Cell Growth by Overexpression of the ZPK Gene. Biochemical and Biophysical Research Communications, 231:153-155, 1997.	
	AS5	Blouin et al., Cell-Specific Expression of the ZPK Gene in Adult Mouse Tissues. DNA and Cell Biology, 15: 631-642, 1996.	
	AT5	Davis, R.J., Human JNK3 Alpha 2 Protein Kinase (JNK3A2) mRNA. GenBank Accession No. U34819, July 25, 1996.	
	AU5	Davis, R.J., Human JNK3 Alpha 2 Protein Kinase (JNK3A2) mRNA. GenBank Accession No. U34820, July 25, 1996.	
	AV5	DeAizpurua et al., Expression of Mixed Lineage Kinase-1 in Pancreatic $\beta$ -Cell Lines at Different Stages of Maturation and During Embryonic Pancreas Development. The Journal of Biological Chemistry, 272:16364-16373, 1997.	
	AW5	Diener et al., Activation of the c-Jun N-terminal kinase pathway by a novel protein kinase related to human germinal center kinase. Proc. Natl. Acad. Sci. USA, 94: 9687-9692, 1997.	
	AX5	Dorow et al., Identification of a new family of human epithelial protein kinases containing two leucine/isoleucine-zipper domains. Eur. J. Biochem, 213:701-710, 1993.	
	AY5	Ezoe et al, PTK1, a novel protein kinase required for proliferation of human melanocytes. Oncogene, 9:935-938, 1994.	
	AZ5	Fan et al., Dual Leucine Zipper-bearing Kinase (DLK) Activates p46SAPK and p38mapk but not ERK2. Journal of Biological Chemistry, 271:24788-24793, 1996.	
	AR6	Fanger, G.R. et al., MEKKs, GCKs, MLKs, PAKs, TAKs, and tpIs: Upstream Regulators of the c-Jun Amino-Terminal Kinases? Current Opinion in Genetics and Development, 7:67-74, 1997.	
	AS6	Glicksman et al., CEP-1347/KT7515 Prevents Motor Neuronal Programmed Cell Death and Injury-Induced Dedifferentiation In Vivo. Journal of Neurobiology. 34: 361-370, 1998.	
	AT6	Glicksman et al., K-252a and Staurosporine promote Choline Acetyltransferase Activity in Rat Spinal Cord Cultures. Journal of Neurochemistry, 61:210-221, 1993.	
	AU6	Hambleton et al., Activation of c-Jun N-terminal kinase in bacterial lipopolysaccharide-stimulated macrophages. Proc. Natl. Acad. Sci. USA, 93: 2774-2778, 1996.	
	AV6	Hirai et al., Activation of the JNK pathway by distantly related protein kinases, MEKK and MUK. Oncogene, 12: 641-650, 1996.	
	AW6	Holzman et al., Identification, Molecular Cloning, and Characterization of Dual Leucine Zipper Bearing Kinase. Journal of Biological Chemistry, 269: 30808-30817, 1994.	
	AX6	Hu et al., Human HPK1, a novel human hematopoietic progenitor kinase that activates the NJK/SAPK kinase cascade. Genes and Development, 10: 2251-2264, 1996.	
	AY6	Ing et al., MLK-3: identification of a widely-expressed protein kinase bearing an SH3 domain and a leucine zipper-basic region domain. Oncogene, 9:1745-1750, 1994.	
	AZ6	Kaneko et al., Neurotrophic 3, 9-bis (alkylthio)methyl - and - bis(alkoxymethyl) -K- 252a Derivatives. J. Med. Chem. 40: 1863-1869, 1997.	
	AR7	Katoh et al., Cloning and Characterization of MST, a novel (putative) serine/threonine kinase with SH3 domain. Oncogene, 10: 1447-1451, 1995.	
	AS7	Kiefer et al., HPK1, a hematopoietic protein kinase activating the SAPK/JNK pathway. EMBO Journal, 15: 7013-7025, 1996.	
	AT7	Knight, E. et al., A Radioactive Binding Assay for Inhibitors of trkA Kinase. Analytical Biochemistry, 247: 376-381, 1997.	
	AV7	Maroney et al., Motoneuron Apoptosis is blocked by CEP-1347 (KT 7515), a Novel Inhibitor of the JNK Signaling Pathway. Journal of Neuroscience. 18(1): 104-111, 1998.	



AW7	Mata et al., Characterization of Dual Leucine Zipper-bearing Kinase, a Mixed Lineage Kinase Present in Synaptic Terminals whose Phosphorylation State is Regulated by Membrane Depolarization via Calcineurin. Journal of Biological Chemistry, 271: 16888-16896, 1996.		
AX7	Nagata et al., The MAP kinase kinase kinase MLK2 co-localizes with activated JNK along microtubules and associates with kinesin superfamily motor KIF3. EMBO Journal, 17: 149-158, 1998.		
AY7	Park et al., Ordering the Cell Death Pathway. J. Biol. Chem. 271(36): 21896-21905, 1996.		
AZ7	Phelps et al., Generation Patterns of Four Groups of Cholinergic Neurons in Rat Cervical Spinal Cord: A Combined Tritiated Thymidine Autoradiographic and Choline Acetyltransferase Immunocytochemical Study. Journal of Comparative Neurology, 273: 459-472, 1998.		
AR8	Pombo et al., Activation of the SAPK pathway by the human STE20 homologue germinal centre kinase. Nature, 377: 750-754, 1995.		
AS8	Qin et al., Nuclear Factor- $\kappa$ B Contributes to Excitotoxin-Induced Apoptosis in Rat Striatum. Molecular Pharmacology, 53: 33-42, 1998.		
AT8	Reddy et al., Cloning of a Novel Putative Protein Kinase Having a Leucine Zipper Domain From Human Brain. Biochemical and Biophysical Research Communication, 202: 613-620, 1994.		
AU8	Sakuma et al., Molecular Cloning and Functional Expression of a cDNA Encoding a New Member of Mixed Lineage Protein Kinase from Human Brain. Journal of Biological Chemistry, 272: 28622-28629, 1997.		
AV8	Sells et al., Emerging from the Pak: the p21-activated protein kinase family. Trends in Cell Biology, 7: 162-167, 1997.		
AW8	Smith et al., Trophic Effects of Skeletal Muscle Extracts on Ventral Spinal Cord Neurons in Vitro: Separation of a Protein with Morphologic Activity from Proteins with Cholinergic Activity. Journal of Cell Biology, 101: 1608-1621, 1995.		
AX8	Su et al., NIK is a new Ste20-related kinase that binds NCK and MEKK1 and activates the SAPK/JNK cascade via a conserved regulatory domain. The EMBO Journal, 16: 1279-1290, 1997.		
AY8	Tung et al., A novel human SPS1/STE20 homologue, KHS, activates Jun N-terminal kinase. Oncogene, 14:653-659, 1997.		

EXAMINER	DATE CONSIDERED
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#EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[NOTE - Must provide a copy of any patent, publication, other information listed, even if it was previously submitted to, or cited by, the U.S. Patent Office in an earlier application, unless the earlier application is identified by the IDS and is relied upon for an earlier filing date under 35 U.S.C. §120, and the copy was provided in the earlier application.]